# UNITED STATES PATENT AND TRADEMARK OFFICE

## BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JEAN-FRANCOIS BACH and LUCIENNE CHATENOUD



Appeal No. 2004-1693
Application No. 08/986,568

HEARD: December 7, 2004

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the examiner's rejection of claims 1, 2, 4-7, 9-13, and 16-18. Claims 1, 2, 4, 5, and 9-12 are representative of the subject matter on appeal and read as follows:

1. A method of treating spontaneous and ongoing auto-immune diseases in humans, comprising administering to a human, in need of such a treatment, a therapeutically effective amount of one or more non mitogenic anti-CD3 active compounds to achieve permanent disease remission through the induction of antigen-specific unresponsiveness, i.e. immune tolerance.

2. The method of claim 1, wherein said non mitogenic anti-CD3 active compound is a non mitogenic anti-CD3 antibody.

4. The method of claim 1, wherein said non mitogenic anti-CD3 active compound is a non mitogenic anti-CD3 monoclonal antibody.

5. The method of claim 1, wherein said non mitogenic anti-CD3 active compound is a non mitogenic anti-CD3 monoclonal antibody $F(ab')_2$ fragment.

9. The method of claim 1, wherein said auto-immune disease is diabetes.

10. The method of claim 1, wherein said auto-immune disease is rheumatoid arthritis.

11. The method of claim 1, wherein said auto-immune disease is psoriasis.

12. The method of claim 1, wherein said auto-immune disease is multiple sclerosis.

The reference relied upon by the examiner is:

Chatenoud et al. (Chatenoud), "Anti-CD3 Antibody Induces Long-Term Remission of Overt Autoimmunity in Nonobese Diabetic Mice," Proc. Natl Acad. Sci. USA, Vol. 91, pp. 123-127 (1994)

Claims 1, 6, 9-13, 17, and 18 stand rejected under 35 U.S.C. § 112, first paragraph (written description). Claims 1, 2, 4-7, 9-13, and 16-18 stand rejected under 35 U.S.C. § 112, first paragraph (enablement). Claims 1, 2, 4-6, 9-13, and 16-18 also stand rejected under 35 U.S.C. § 103(a). The examiner relies upon Chatenoud as evidence of obviousness.

We affirm the written description rejection and reverse the enablement and obviousness rejections. We also enter a new ground of rejection under 37 CFR § 41.50(b).[1]

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[1] Appellants also raise an issue in regard to the propriety of the examiner reopening prosecution after a previous decision of the Board in which a new rejection was introduced by the merits panel under the then existing provisions of 37 CFR § 1.196(b) that was subsequently overcome by way of amendment. Appeal Brief, pages 3-5. However, that issue is subject to administrative review by way of petition and is not an appealable issue. In fact, appellants filed a petition in this regard, Paper No. 30, received December 10, 2002, that was denied. See Paper No. 32.

## Background

The present invention is directed to a method of treating spontaneous and ongoing auto-immune diseases including diabetes, rheumatoid arthritis, psoriasis, and multiple sclerosis. See, e.g., claims 1, 9, 10, 11, and 12. As described in the specification, the treatment involves "a therapeutically effective amount of one of more non mitogenic anti-CD3 active principles to achieve permanent disease remission . . .." Id., page 3. The preferred non mitogenic anti-CD active principles are stated to include anti-CD antibodies or fragments thereof. Id.

The work described in this application is an extension of the work set forth in Chatenoud, the reference relied upon by the examiner as evidence of obviousness. Chatenoud is stated to describe "complete and durable remission of the spontaneous auto-immune diabetes, in overtly diabetic NOD (non obese diabetic) mice." Specification, page 1. An anti-CD3 monoclonal antibody was used in the experiments reported to result in remission of diabetes. Chatenoud, paragraph bridging pages 125-126. Appellants explain the present invention as follows:

> By further investigating the mode of action of anti-CD3 mAb in this model, the inventors have found that the long term effect was obtained only when treating animal at a very advanced disease stage, i.e. overt autoimmunity. They also demonstrate that non mitogenic, $F(ab')_2$ fragments of the entire CD3 mAb, that are much better tolerated than the whole entire CD3-mAb, also afford a long term in vivo effect in overtly diabetic NOD mice as did the whole anti-CD3 mAb.
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> This finding is an unexpected extension of the published data which until now, in both transplantation and antigen and/or pharmacologically induced auto-immunity, has proposed $(Fab')_2$ fragments of anti-CD3 mAb as effective tools to only achieve immunosuppression (an overall depression of immune responses that is only maintained through the chronic administration of the drugs), but not to promote permanent antigen-specific unresponsiveness namely, a state of immune tolerance

(an antigen-specific immune unresponsiveness that is maintained in the absence of chronic generalized immunosuppression).

Specification, pages 1-2.

## Discussion

1. Written Description.

The examiner questions whether the genus of non mitogenic anti-CD3 active compounds required by claim 1 on appeal complies with the written description requirement of § 112, first paragraph. The examiner has determined that the only compounds described in the specification are anti-CD3 antibodies and fragments thereof. Examiner's Answer, page 4. The examiner states "the appellant has disclosed no other type of compound which, like an anti-CD3 antibody, is capable of binding to CD3 in a ligand-receptor manner [.] Appellant has merely described the genus by functional language [and] has failed to describe any type of common structure that such a genus of compounds must have in order to bind to the CD3 antigen." Id.

In response, appellants do not contest that the specification only describes non mitogenic anti-CD3 antibodies or fragments thereof as the "active compounds" required by claim 1 on appeal. Rather, appellants' only argument in response to this rejection is "throughout the specification and prosecution history, the term 'anti-CD3 active compound' is used to denote non-mitogenic, anti-CD3 antibodies or fragments thereof." Appeal Brief, page 5 (footnotes omitted).

To read the generic term "non mitogenic anti-CD3 active compounds" as used in claim 1 on appeal to be limited to non mitogenic, CD3 antibodies or fragments thereof

as appellants would have us do would be improper. As explained in In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989):

> [D]uring patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed. . . . An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.

Appellants describe in the specification the use of a broad class of "non mitogenic anti-CD3 active principles." Anti-CD3 antibodies and fragments thereof are described as being a preferred embodiment. The claims on appeal are drafted consistent with the description of the invention in the specification with claim 1 directed to the generic invention and certain of the dependent claims directed to preferred embodiments. Compare claim 1 with dependent claims 2, 4, 5, and 16. We see no reason why the public should need to comb through the administrative file if a patent were to issue with the claims as presently drafted in order to understand that the broad term "non mitogenic anti-CD3 active compounds" as used in claim 1 on appeal actually means "non-mitogenic, anti-CD3 antibodies or fragments thereof" as argued by appellants in the Appeal Brief. Rather, the appropriate course of action is for appellants to amend claim 1 during the examination process to reflect their argument.

The examiner's rejection under 35 U.S.C. § 112, first paragraph (written description) is affirmed.

2. Enablement.

The basis of the examiner's rejection is that appellants have not "enabled the treatment of the established autoimmune disease in humans." Examiner's Answer,

page 5. The examiner acknowledges the work set forth in the specification based upon NOD mice and considers that it "would be unpredictable as to whether or not such treatments would also be efficacious in humans." Id.

Appellants argue that NOD mice have been studied extensively as a model of insulin-independent diabetes mellitus (IDDM), Appeal Brief, page 7, and cite In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995) in support of their position. Id. In response, the examiner states that "appellant[s] must jump through a higher hoop to establish enablement than did Brana." Examiner's Answer, page 11.

We disagree with the examiner that appellants have to jump through a higher hoop than did the applicants in Brana. There is a single patent law and each claim's patentability is determined in light thereof. In reviewing the examiner's reasons for holding the claims to be non-enabled, we find Brana to be particularly instructive. The court stated, "it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment of humans." Brana, 51 F.3d at 1568, 34 USPQ2d at 1442.

Example 1 of the specification describes experiments where overtly diabetic NOD mice were treated with $(Fab')_2$ fragments of anti-CD3 mAb. Appellants conclude in regard to the results of Example 1 that "$(Fab')_2$ fragments of the mAb appeared potent in promoting permanent remission of overt diabetes in the conditions of the experiments." Specification, page 7. Appellants have also relied upon references stated to show that NOD mice are standard laboratory animals in this art. Appeal Brief,

pages 6-7. The examiner seems to agree that NOD mice are a model for human diabetes. Examiner's Answer, page 9. Thus, the examiner's concern is seen as one in regard to the claimed therapy being effective in humans. However, Brana clearly states that enablement in this field does not require that the compound be ultimately shown to be useful in humans.

On this record, we reverse the enablement rejection.

3. Obviousness

We reverse this rejection as it is based upon an incorrect assessment of the facts described in Chatenoud by the examiner. The key finding made by the examiner in support of this rejection is that Chatenoud teaches "treatment of NOD mice having an overt/established autoimmune disease (diabetes) via injection with a purified, endotoxin-free, monoclonal anti-CD3 F(ab')[$_2$] fragment." Examiner's Answer, page 6. This is incorrect.

The work relied upon by the examiner is set forth in the paragraph bridging pages 125-126 of Chatenoud wherein treatment of NOD mice exhibiting overt diabetes with "antiCD3" is described as resulting in remission of diabetes. The examiner states that he "cannot determine whether or not recitation of 'anti-CD3' in the reference refers to the whole antibody, or was merely a short hand notation for its fragment." Examiner's Answer, page 12. In our view, reading Chatenoud in its entirety leads to the conclusion that the use of "anti-CD3" in this passage refers to the whole antibody, not a fragment.

Chatenoud does describe the use of anti-CD3 F(ab')$_2$ fragments. See, e.g., Chatenoud, page 123, "MATERIALS AND METHODS" ("Anti-CD3 F(ab')$_2$ was

prepared....") It appears that Chatenoud uses the nomenclature anti-CD3 $F(ab')_2$ whenever the fragment was used and anti-Cd-3 when the whole antibody was used. Compare Figures 2a and 2b with Figures 2c and 2d where "Anti-CD3" was used in the former and "$F(ab')_2$ Anti-Cd3" was used in the latter. This reading of Chatenoud is supported by the description of Chatenoud and the present invention in the specification. Id., pages 1-2. Appellants describe Chatenoud as using low doses of an anti-CD3 monoclonal antibody and that the use of non-mitogenic $F(ab')_2$ fragments to treat animals in that model was developed later and forms part of the present invention.

Where as here the examiner's conclusion of obviousness is premised upon faulty fact-finding, the rejection cannot be sustained. Accordingly, the rejection under 35 U.S.C. § 103(a) is reversed.

NEW GROUND OF REJECTION UNDER 37 CFR § 41.50(b)

Claims 1, 2, 4-7, 10-13, and 16-18 are rejected under 35 U.S.C. § 112, first paragraph(enablement).

These claims are directed to treatment of auto-immune diseases in general or to rheumatoid arthritis, psoriasis or multiple sclerosis in particular.

"Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" In re Wright, 999F.2d 1557, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)(citations omitted). As noted in In re Wands, 858 F.2d 731, 736, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988) (footnote omitted):

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd. Pat App. & Int. 1986)]. They

> include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

Here, the specification provides little if any guidance as to how autoimmune diseases are to be treated using "anti-CD3 active compounds" in general as required by claim 1. Nor is there evidence or prior art cited in the specification that anti-CD3 active agents were known to be useful in treating auto-immune diseases in general or the three specific conditions set forth in claims 10-12 at the time of the present invention. As previously noted, claim 1 is open to treating any autoimmune disease using "non mitogenic anti-CD3 active compounds." The dependent claims either narrow the non mitogenic compound or the disease to be treated, but not both. Thus, the claims are quite broad. Furthermore, these claims are directed to the highly unpredictable field of treating autoimmune diseases.

In considering the Wands factors, we find that the only one weighing in favor of appellants is the level of skill in the art, which is quite high. However, considering all of the factors together we conclude that they weigh in favor of a conclusion of lack of enablement for these claims. On this record it is reasonable to require appellants to submit "suitable proofs indicating that the teaching contained in the specification is truly enabling." In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

TIME PERIOD FOR RESPONSE

Regarding the affirmed rejection, 37 CFR § 41.52(a)(1) provides "[a]ppellant may file a single request for rehearing within two months from the date of the original decision of the Board."

In addition to affirming the examiner's rejection of one or more claims, this decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) Reopen prosecution. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
>
> (2) Request rehearing. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

Should the appellants elect to prosecute further before the examiner pursuant to 37 CFR § 41.50(b)(1), in order to preserve the right to seek review under 35 U.S.C. §§ 141 or 145 with respect to the affirmed rejection, the effective date of the affirmance is deferred until conclusion of the prosecution before the examiner unless, as a mere incident to the limited prosecution, the affirmed rejection is overcome.

If the appellants elect prosecution before the examiner and this does not result in allowance of the application, abandonment or a second appeal, this case should be returned to the Board of Patent Appeals and Interferences for final action on the affirmed rejection, including any timely request for rehearing thereof.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN PART; 41.50(b)

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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